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SOME OBSERVATIONS UPON THE RÔLE OF IMMUNITY IN TUBERCULOSIS.*

BY HENRY F. R. WATTS, M.D., BOSTON,

Physician to Convalescent Home of Boston City Hospital; Instructor in Theory and Practice of Medicine, Tufts College Medical School.

WHILE on active service with the Medical Corps of the Army during the late war, the writer was assigned to the Tuberculous Section of the Division of Internal Medicine. This inforced concentration upon tuberculosis, together with the opportunity of carrying on the work, under the supervision of Colonel George E. Bushnell, chief of the section, whose profound knowledge and boundless enthusiasm were an inspiration to every man in the section, had the effect of developing a renewed interest in the subject of tuberculosis.

When one thinks tuberculosis, one thinks in terms of immunity, and it is my intention to present in this paper some of the current views upon the rôle of immunity in tuberculosis.

It has long been known that the great majority of the human family acquires tuberculosis in some form at some time. "Every man has a little tuberculosis," is an old proverb, the truth of which seems to have been established by many and repeated observations. If this is true, why does not the majority of the human race die of tuberculosis? Of course the answer to this is that the majority of the race is protected by its immunity.

Immunity carries with it as a corollary, localization. Localization is always a sign of immunity. If a man cannot localize pus germs he dies of septicaemia. If he does localize them he has an abscess. If his immunity is of a high degree, he has no suppuration. If an individual has no immunity to the pneumococcus and becomes infected with that organism, he dies of pneumococcus septicaemia. It is a sign of a degree of immunity when pneumonia occurs.

If a guinea pig is given a large injection of tubercle bacilli he quickly dies of a generalized tuberculosis, because he has no immunity. This is primary tuberculosis. If, however, the pig is inoculated with a smaller number of the organisms, he does not die; but, on the contrary, he acquires a degree of immunity to the disease, and can be reinfected only with difficulty, depending upon the degree of his acquired immunity and the size of the dose of organisms administered.[1]

There is a natural immunity which varies in every species of animal, including man, and in the individual of each species, but in the case

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of tuberculosis it is not sufficiently strong to afford any material protection to good-sized doses of tubercle bacilli.

It is well to remember that immunity is always relative and that complete immunity to any disease does not exist.

Immunity, as the term is used by the writer, in connection with tuberculosis, refers to an acquired resistance to the disease.

Localization being an indication of immunity, it follows that phthisis, or tuberculosis localized in the lungs, presupposes a certain degree of immunity, acquired immunity, which could only have been acquired by an initial or primary infection occurring at some remote time in the past.

The results of animal experimentation, and in the absence of human experimentation, observation of the course of the disease as it occurs spontaneously in man, have established the theory, now generally accepted, that phthisis is a late manifestation of tuberculosis acquired during childhood. Behring, Romer, Hamburger, and others, basing their opinions upon the results of animal experimentation, maintain that primary infection cannot result in phthisis. Either the primary infecting organisms are impounded in the lymphatic system where they remain indefinitely and so react upon the tissues of the body as to develop more or less immunity, or they are freely disseminated throughout the body, resulting in a general miliary tuberculosis which is fatal.

The ubiquity of the infecting agent, the tubercle bacillus, in civilized countries is an hypothesis which few will find difficulty in accepting. It is estimated, for instance, that the number of bacilli discharged daily in the sputum of an advanced consumptive equals the number of human beings of the globe.

There is undoubted evidence that the human body is exceedingly prone to tuberculous infection. "Every man has a little tuberculosis," and when these circumstances are considered, it does not seem surprising that one out of every eight in civilized countries succumbs to the disease, but rather that the seven escape.

Authorities are agreed that the new-born infant, even that of a tuberculous mother, is free from tuberculosis; is virgin soil, ready and waiting for the ubiquitous seed. In civilized countries the soil does not have to wait long for the seed. Few escape.

It may well be asked, how is it that we know that tuberculosis is so widespread in civilized man as to be practically universal. There are two chief sources of information: the tuberculin test and the result of autopsy. Clinical observation is also an important source of information.

When the human body becomes infected by the tubercle bacillus, it becomes sensitized to tuberculin and "reacts" to tuberculin, the degree of sensitization being somewhat related to the degree of resistance or immunity which the body has acquired. Those who have no immunity, as the new-born baby, and the advanced consumptive whose immunity has utterly failed and who is going rapidly to the bad, do not react to tuberculin, even in large doses.[2]

When Koch began studying the properties of tuberculin, our present day views upon the subject of immunity were undeveloped, and as a result of his observations, he arrived at the conclusion that all tuberculous subjects would react to a dose of ten milligrams or less. In his own case, he reacted to 25 mg., and he established this as the standard for the healthy man, saying, that tuberculous cases would react to 10 m.g., and non-tuberculous cases to 25 m.g. At a later date, however, it appeared that Koch himself had tuberculosis. The fact that he did not react until a dose of 25 m.g. was reached, was evidence that he had a high degree of immunity, not that he had no tuberculosis.

It is believed that every adult will react to tuberculin if it is given often enough and in sufficiently large dose.

A reaction to tuberculin is considered as absolute evidence that the subject has been infected with the tubercle bacillus, because humans who have not been thus infected, will take any quantity of tuberculin without reacting. Young infants have been given several grams without producing a reaction. When it is considered that a thousandth of a milligram often produces a reaction, the significance of the massive dose to the non-tuberculous infant without reaction, can be better appreciated.

A certain Austrian regiment was tested with tuberculin and 60% reacted positively. Most of these men were healthy at the time and remained healthy for years, the percentage of tuberculosis developing among them was not greater than the average in the general popu-

lation of that region. The experiment aroused much interest at the time; but in the light of the present conception of the subject, the interest of it centers in the 40% who did not react. It is explained by a higher immunity in the 40%, and if they had received a large enough dose, they would also have reacted.

The facts concerning the reaction of children to tuberculin are based largely upon the observations of von Pirquet, who showed that about 90% of the children of Vienna who were under 14 years of age, reacted positively to the cutaneous test. It was thought that the 10% of negatives were non-tuberculous. Recalling Koch's observations upon his own reactivity, the question naturally arises: were the 10% of negatives non-tuberculous, or were they tuberculous with so high a degree of immunity as to preclude reaction to this test?

Of course it is no longer held that a positive tuberculin reaction indicates tuberculous disease. It really means a degree of immunity, and immunity, as we have seen, can be acquired only by previous tuberculous infection. A sharp distinction should be drawn between tuberculous infection and tuberculous disease.

Post-mortem findings have demonstrated the presence of tuberculosis in some form in a high percentage of all cases coming to autopsy. Observers have not all arrived at the same figures, variations possibly being more or less governed by the zeal of the pathologist in searching and recording. It is not difficult to imagine the possibility of minute and obsolete lesions escaping observation. It seems hardly necessary to present a detailed review of the data available in the literature of this phase of the subject.

Few, if any, civilized countries, especially those in large centres, escape tuberculous infection. It does not necessarily cause any sickness or other evidence of its presence than an altered reactivity to tuberculin. Every man who is brought under civilized conditions, has come in contact with the tubercle bacillus and has taken them unto himself as the magnet does the steel, and has thereby undergone a sort of vaccination. The man whose vaccination has been more or less of a failure is the one who develops tuberculosis.

Investigation has shown that the child at a very early age begins his vaccinating process. It has been observed that in a family of healthy children who become exposed to tuberculosis by a consumptive coming to live in the house, the children over four years were unaffected by the direct exposure, while those under that age suffered an impaired development and were less robust than the elder brothers and sisters. The inference was that those children who were over four years old had already undergone their vaccination and were immune, while the younger children were apparently hard-hit by the infection to which they were exposed and against which they were not yet sufficiently protected. However much or little this observation proves, the general belief now is that the child acquires his infection at a very early age, during the "dirty age," so called, when he is creeping on the floor and putting everything into his mouth; sucking toys carved by a consumptive German, maybe, painted by another consumptive, and wrapped by a third. A family history of tuberculosis means little but an undoubted opportunity for infection, but the absence of such a family history also means little. Every child has an abundant opportunity for infection. Children in healthy surroundings have a better chance of getting a small infection and better vaccination.

The baby who is exposed to the cough of a tuberculous mother or nurse is in danger of receiving a massive dose of organisms, larger than what might be called the normal immunizing dose, and dies of general tuberculosis; general, because there is not likely to be present the necessary immunity to bring about localization. Holt and others give instances of tuberculous infection of the wound from a tuberculous operator during ritual circumcision of the Jews. The infant promptly becomes sick with tuberculosis, miliary in character, which runs an acute, rapid and fatal course.

A word about sensitization: Calmette of Lille found that if an animal is given a single small injection of tubercle bacilli, it would develop a marked immunity; but if it were given a number of small injections at frequent intervals, it died more quickly than the unprotected animal, showing that reinfection in the period of sensitization, immediately after the primary infection, is a peculiarly deadly thing. Sensitization, however, is an early phenomenon after primary infection and may be disregarded in the adult consumptive and in those giving evidence of having established an immunity.

We have no means of measuring the size of the infecting dose of bacilli which, in the child, acts beneficially in developing immunity without developing disease. It is well established, however, that minute doses acquired during the dirty age do result in establishing an immunity, and that opportunities for the acquisition of a greater degree of infection during that period may result in generalized tuberculosis.

Bushnell holds that, once tuberculous, always tuberculous; that once living tubercle bacilli gain entrance to the body, they or their progeny remain in the body in a living state, and so promote and maintain immunity. If the tuberculous subject were capable of entirely curing and eradicating his tuberculosis, he would, by gaining freedom from his tuberculous infection, lose his immunity, and thus render himself susceptible to a new infection which might conceivably be worse than the first.[3]

A vast deal of work has been done in an endeavor to determine the channel of entry into the body of the infecting agent. Popular belief based upon popular exploitation of the subject, disposes of the question with very little difficulty; if the infecting agent is human tuberculosis, it is inhaled; if bovine, it is ingested. Experimentation has shown that there are three channels of entry; the respiratory tract, the alimentary tract, and by inoculation into the skin and mucous membrane. There is no agreement among authorities as to the most common channel, and the evidence in literature covering the point is very voluminous. It seems doubtful, however, if tubercle bacilli ever reach the alveoli of the lungs by the air route, except under most extraordinary conditions, and if they do there is good evidence to show that the tubercle does not primarily develop at this point. The primary infection, if localized, is likely to be confined to the lymphatics. This has been demonstrated by necropsies of children in whom glandular involvement always occurs before the lungs are attacked, unless it be a generalized tuberculosis occurring before an immunity has been developed. In adults, with phthisis, the bronchial and mediastinal glands always show evidences of a very early involvement. These glands may have been infected primarily by an invasion by any one of the three channels mentioned.

Phthisis is an outgrowth of the primary glandular focus and again (at the risk of being tiresome) it must be stated that phthisis, or pulmonary tuberculosis, is a localization of tuberculosis and, as such, is an expression of immunity.

Miliary tuberculosis, on the other hand, is the antithesis of phthisis and occurs only in the absence of immunity; either before an immunity has been acquired or after it has completely broken down. It is common to see at autopsy of cases dying of phthisis (and in the army we autopsied every case that died) fresh miliary tubercles in the lungs, liver, spleen and kidneys, indicating a fresh miliary tuberculosis. This does not mean that the patient died of miliary tuberculosis, but that his immunity had gone and that he developed his miliary tuberculosis for the same reason that he died.

It was formerly held by pathologists that the presence of tubercle bacilli in the blood stream was evidence that the patient was in the greatest danger of developing generalized tuberculosis. Long experience, however, has shown that it is not at all unusual to find tubercle bacilli circulating in the blood of individuals who have not and do not develop very severe tuberculosis. This is accounted for by the patient's immunity.

At the present state of our knowledge, the following conclusions of Romer seem to be justified; they at least, enjoy a general acceptance among present-day students of the subject: Tuberculous infections occurring during childhood, so long as they are not acute and fatal immediately, endow the organism with a heightened resistance against renewed infection with tubercle bacilli. Immunity thus produced is, as a rule, sufficient to protect the person against exogenic infection during after years. When, however, extraordinary physiological or pathological conditions permit the bacilli, harbored within the body, to proliferate because of the inadequacy of the failing immunity, which becomes incapable of preventing metastatic reinfection, new tuberculous foci are formed, and again, or perhaps for the first time, clinical phenomena of disease make their appearance.

Experience shows that the metastatic reinfections mostly occur in individuals who were subject to massive infections during childhood. Therefore, "phthisis is but the last verse of the song, the first verse of which was crooned to the infant in the cradle."

The enthusiasts are strong for the theory that exogenic infection of the adult in civilized countries does not and cannot occur and that the average adult who must have acquired his immunity in childhood, or he could not have attained to adult life in the presence of the ubiquitous infecting agent, has nothing to fear from contact infection, even should he eat tubercle-laden sputum.

There is much evidence in support of the holdings of these enthusiasts and we look to experience in sanatoria and other congregating places of consumptives for data. Thousands of men and women engaged in a sanatorium work, as doctors, nurses, orderlies, and others, do not show a higher incidence of the disease than do persons of other occupations, yet the opportunities for infection of the susceptible are abundantly present. If guinea pigs, caged, are kept in a scrupulously clean tuberculosis ward, they promptly contract tuberculosis.[4] The consorts of married consumptives do not develop the disease in greater proportion than occurs among others of like social stratum.[5]

For many years before the tubercle bacillus was discovered, and consequently before any ideas as to prevention of infection were in general force, the little town of Lippspringe, in Germany, has been a mecca for consumptives. In 1820, its permanent population was 1,100. In 1909, it was 3,473. During this time, thousands upon thousands of open cases of tuberculosis have congregated at this place for the cure. The peculiar development of the resort did not, at first, lead to the building of large hotels and sanatoria, but the permanent population received the visiting consumptives into their homes, and for the most part, the family attended to the housework and did the nursing. Few domestic servants and, of course, no nurses, were in requisition. The population of the place has been very stable, few emigrated, and there were few new comers. The hygiene of the homes and of the town must have been medieval. For the decision of the question as to the danger of contact infection, it may be affirmed that at no time and no where in the world has a natural experiment of such extent and such duration been made as here.[6]

From the circumstances set forth above, it follows with certainty that if the views which we were preaching not so very long ago were true, there would long since have been no permanent population of Lippspringe. What was the result? In the first two decades of the last century the annual average deaths from tuberculosis was 10 per 1,000 population. In the decade from 1875 to 1885 it was 8 per 1,000. In the following decade it was 7 per 1,000.

Bushnell, together with others, says that transmission of pulmonary tuberculosis, at least to adults, through transient association with that disease, does not exist and never has existed.[7]

It is well known that aboriginal peoples have no tuberculosis in their native habitats and so do not acquire the childhood immunity infection. When these people come under the influence of civilized conditions, their mortality from tuberculosis is proverbial and the character of their disease is apt to be of the acute and rapid type.

The further one goes from civilization, the more rare is tuberculosis and at the same time the more virulent it is when it occurs. Per contra, where tuberculosis abounds, the less severe, on an average, are the individual cases, which is another way of saying: where tuberculosis abounds the more opportunity there is for acquiring an early immunity.

In view of all the facts, figures and opinions, as above set forth, it would seem to be in order to inquire as to the results of the anti-tuberculosis campaign which we have been waging in recent years. There has been an undoubted decrease in the occurrence of the disease in many of our cities and elsewhere, but the decrease has not kept pace with the decrease in the general mortality.[8] Moreover, the decrease, where it has occurred, began to take place before we began our campaign. It must be confessed that the results of the campaign have been somewhat disappointing to those most active in the movement.

An analysis of available data shows that there is a striking correlation in time between urbanization and the progress of industrialism, and the death rates from phthisis. Wherever urbanization is new, wherever modern industries have been recently developed, the death rate has been rising. This is true in Japan, Norway, Ireland, Serbia, and elsewhere. Ireland, for instance, as a whole, shows a gradual rise from 1870 to 1895, while Belfast, long an industrial centre, has shown a steady decline from 1885 to 1910.

Wherever industrial conditions have obtained for several generations, the death rate has been declining. In England, where the decline has been more pronounced than in any other country, the decline began to take place in 1833 and has continued ever since.[9] The beginning of the nineteenth century was the period of England's industrial development, and here the decrease in the death rate from phthisis has been contemporaneous with the adaptation of a people to urban life.

There are so many factors entering into this complex problem, which still remain obscure, it is difficult to arrive at satisfactory conclusions. It would seem that recent improvements in the social and hygienic conditions of the working classes, who constitute the majority of the candidates for the disease, must be a factor in future, if not in present tuberculosis morbidity and mortality. But the adaptation of people to city life and to the tubercle bacillus, is perhaps of greater importance than all other factors taken together, in bringing about the mortality reduction which has occurred.

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THE SCHICK TEST AND IMMUNIZATION WITH DIPHTHERIA TOXIN-ANTITOXIN

BY BENJAMIN WHITE, PH.D., BOSTON,

Director, Division of Biologic Laboratories, Department of Public Health, Commonwealth of Massachusetts.

THE prevention of diphtheria, and even its eradication among the permanent population of the Commonwealth of Massachusetts, is possible of accomplishment. We now have at our disposal, in addition to the established antitoxin treatment, not only a reliable method for determining the susceptibility of human beings to diphtheria, but also a simple and safe procedure for rendering susceptible individuals immune to this disease.

Diphtheria, in 1919, was responsible for 14.9 deaths per 100,000 population, or a total of 591 deaths out of 7,928 reported cases in this State. It is reasonable to assume that all cases were not reported. In addition to the toll of 591 lives we suffer great economic loss, anxiety, and time entailed in the sickness and treatment of 8,000 persons. Moreover, diphtheria is essentially a disease of childhood, and the State is yearly deprived not only of approximately 600 prospective citizens, but also of their possible contribution as potential parents.

We still have an incidence of about 8,000 cases and a mortality of approximately 8 per cent. of all reported cases in spite of the complete efficacy of antitoxin treatment when promptly and properly applied. Antitoxin, when given in sufficient amounts on the first day of the disease, in cases without serious complications, effects 100 per cent. of recoveries. With the possession of such an efficient means of treatment, it would be difficult to understand why we continue to have deaths from diphtheria were it not for the astonishing facts revealed in Carey's investigation of the circumstances attending 1,000 deaths from this disease. He found that "31.5 per cent. of these deaths occurred in individuals who had been sick one week or more without medical attention; 11.8 per cent. occurred in individuals who were moribund at the doctor's first visit; 7.6 per cent. occurred in individuals in whom the condition was unrecognized until it was too late for the antitoxin to be efficacious, and 65 per cent. of these deaths occurred in children who were 5 years or under."

The causes for the prevalence of diphtheria with its stationary death rate are:

1. The presence of susceptible individuals in every community and failure to detect and immunize them.

2. The existence of healthy human carriers of virulent diphtheria bacilli.

3. The neglect of parents or other temporary or permanent guardians to procure medical attention for children in the early stages of the disease.

4. The failure to report some cases of diphtheria.

5. The failure to diagnose diphtheria in its early stages.

6. The failure of some physicians (a) to administer antitoxin in suspicious cases before making a definite diagnosis; (b) to avail themselves of the diagnostic facilities offered by the

State and various cities; and (c) to administer antitoxin early enough or in sufficient amount, or (d) to administer antitoxin intravenously in late or severe cases.

It must be apparent that by detecting all susceptible persons in every community and rendering them immune to diphtheria the other causes for the present continued morbidity and mortality from this disease would eventually cease to operate.

I. THE PRESENCE AND DETECTION OF PERSONS SUSCEPTIBLE TO DIPHTHERIA INFECTION.

As a result of the work of Schick, we know that individuals who possess less than one-thirtieth unit of diphtheria antitoxin in one cubic centimeter of their blood may, and frequently do, contract diphtheria if exposed, while those possessing this or a larger amount of antitoxin rarely, if ever, develop clinical diphtheria. The earlier methods for determining the antitoxin content of the blood were far too intricate to permit of their clinical application. In 1913, however, Schick described a simple test for this determination. Following the introduction of this method, Park, Zingher, and others carried out investigations on the susceptibility or immunity of various age groups, and the figures recently published by Park may be taken as indicating the percentage of individuals liable to contract diphtheria.

SUSCEPTIBILITY OF VARIOUS AGES TO DIPHTHERIA.

AGE	SUSCEPTIBLE
Under 3 months	15%
3 to 6 months	30%
6 months to 1 year	60%
1 to 2 years	70%
2 to 3 years	60%
3 to 5 years	40%
5 to 10 years	30%
10 to 20 years	20%
Over 20 years	12%

From this table it is apparent that the majority (85 per cent.) of infants under three months of age are immune to diphtheria and that the percentage is practically the same as in adults. This may be explained by the theory that babies are born with a passive immunity acquired from the mother through the placental circulation. But this immunity disappears to a considerable extent with the succeeding months, resulting in the susceptibility of about 70 per cent. of all children between one year and two years of age. The age of greatest susceptibility is from six months to five years, which corresponds closely to the age groups in which the most dangerous laryngeal forms of diphtheria and complicating bronchopneumonias occur. As the age increases, the proportion of susceptibles decreases, which also squares with the lower incidence of diphtheria in the higher age groups.

1. *Theory of the Schick Test.* Diphtheria toxin causes an inflammatory action when injected into susceptible tissues. This reaction does not occur if the toxin is neutralized with its antitoxin before injection, or if an adequate amount of antitoxin is already present in the blood of the individual. Schick found that an antitoxic content of one-thirtieth unit per cubic centimeter of blood is ample, not only to render one immune to infection, but also to neutralize and prevent the inflammatory action of a small amount of toxin injected into the skin. Upon this phenomenon is based the Schick test. A positive reaction means susceptibility, a negative reaction shows immunity. Those who show a positive reaction may and do contract the disease; those who show a negative reaction may become carriers of virulent diphtheria bacilli, but do not develop clinical diphtheria.

2. *Technic of the Schick Test.* The test is carried out by injecting intracutaneously one-fiftieth of a minimum lethal dose (M. L. D.) for a guinea pig weighing 250 grams. The State Department of Public Health supplies free an outfit, which contains sufficient titrated diphtheria toxin with the proper amount of sterile salt solution for fifty tests. The toxin is contained in a capillary tube, and when it is desired to perform the test the contents of the tube are expelled into the bottle containing the salt solution. One-tenth of a cubic centimeter of this mixture represents the dose to be injected into the skin and contains one-fiftieth M. L. D. of toxin. This diluted toxin must be used within a few hours after mixing, because it rapidly loses its potency when exposed to light and room temperature. The skin on the flexor surface of the arm, preferably above the elbow, is cleansed with alcohol, acetone or ether, and one-tenth cubic centimeter of the diluted toxin is injected *into* the epidermal layers of the skin. This is best accomplished by means of a short but sharp-pointed No. 26 or 27 gauge hypodermic needle. The 1 c.c. "Record," or other tuberculin syringe, is well adapted for the purpose. If the

point of the needle has been properly inserted with the lumen uppermost and visible through the skin, the injection should produce a small, slightly raised, white area, or wheal, which should move with the skin and disappear in about one-half hour. The injection should never be made *under* the skin. The technic of the test is easily acquired. The injection causes little or no pain, it is never followed by constitutional symptoms, and the site of injection requires no subsequent care.

3. *The Positive Reaction.* A positive reaction begins to appear in 24 to 36 hours and is characterized by a circumscribed area of redness and slight infiltration which measures one to two centimeters in diameter. It develops gradually, reaches its greatest intensity on or about the fourth day, then fades very slowly, leaving a scaly, brownish pigmented spot. The positive result of the test represents the true irritant action of diphtheria toxin, and signifies that the individual possesses little or no antitoxin in the blood, and therefore may contract the disease.

4. *The Negative Reaction.* The native diphtheria antitoxin in the tissues of an immune person neutralizes the injected diphtheria toxin, and on the day following the injection no signs are present except the slight and fleeting mark incident to the insertion of the needle.

5. *The Pseudo-Reaction.* In some individuals, particularly in adults, a reaction develops which may be confused with a positive reaction. Owing to the hypersensitiveness of some persons to the protein of the diphtheria bacillus present in the toxin, a local reaction may appear at the point of injection. The pseudoreaction is distinguished from the positive reaction by its more rapid development. "It appears usually within twelve to eighteen hours, and fades in about three to four days, leaving only an irregular area of brownish pigmentation and generally shows no scaling. In appearance the moderate pseudoreactions, at the end of twenty-four hours, resemble very much the fully developed positive reactions, while the marked pseudoreactions show a considerable amount of infiltration with a central darker reddish area, surrounded by a fainter areola, which shades off into the surrounding skin" (Zingher). In order to exclude pseudoreactions, repeated observations over a period of five or more days should be made and the appearance carefully noted. "By this time the pseudoreaction will have faded and can be recognized by a blotchy area of pigmentation, while the true positive reaction will be at its height. The positive reaction will show at this time a definite circumscribed area of scaling redness, which gradually develops a brownish pigmentation. Those tests, however, which show only an area of bluish discoloration, or faded irregular areas of brownish pigmentation which do not scale, are generally the remains of pseudoreactions" (Zingher).

A control test should be performed on the other arm, injecting one-tenth cubic centimeter of a similar dilution of toxin which has been heated to 75° C. for five minutes. "By heating the toxin broth at this temperature the soluble toxin is destroyed, while the autolyzed protein of the diphtheria bacillus, which causes the pseudoreactions, is not appreciably affected. The control test with the heated toxin will reveal the pseudoreaction and combined reactions. Observations must be made at the end of seventy-two or ninety-six hours. The twenty-four-hour reading will give fairly accurate results in about 95 per cent. of the tests, when the control test with heated toxin has also been made. If negative, both the test and control will be normal. If a pseudoreaction is present, both the test and the control will show areas of redness and infiltration, which are similar in size and appearance; both reactions will fade at the end of seventy-two hours and leave only a small, irregular area of pigmentation, and generally no scaling. The pseudoreaction varies in intensity in different individuals from an area of circumscribed redness without infiltration to a reaction which shows a considerable degree of redness and infiltration, and a more or less characteristic clinical appearance."

6. *The Combined Reaction.* "If a combined reaction is present, the redness and infiltration at the site of the Schick test will be more marked at the end of twenty-four hours than in the control test. At seventy-two hours, the positive reaction will be quite distinct, while the control test will show only a blotchy area of pigmentation representing the pseudoreaction elements of the test. If the test is positive, the reaction at the end of twenty-four and seventy-two hours will be positive only at the site of the Schick test. The negative and the pseudo-

reactions indicate immunity, the positive and the combined reactions, susceptibility of diphtheria" (Zingher). The appearance of pseudo-reactions presents no especial difficulties. A short experience in reading the reactions will suffice to enable one to make a correct interpretation of the results.

7. *Importance of the Schick Test.* The importance of this test cannot be too strongly emphasized. The information which it yields as to the susceptibility of an individual enables us to apply a method for transforming susceptibility into immunity, thus protecting that person against a possible attack of diphtheria.

The immunity possessed by persons giving a negative Schick reaction obviates the necessity of administering antitoxin to them even though they are exposed to infection. Park states, "It seems safe to rely on the belief that a person with a sufficient amount of antitoxin to give a negative Schick test is incapable of developing constitutional toxaemia, or a severe infection from diphtheria bacilli. There is a doubt as to whether very slight infections of the superficial mucous membrane may occur in such persons. My own opinion is that cases supposed to be of this character are instances of streptococcus infection, the diphtheria bacilli being present as in a carrier. Those that show a faintly positive Schick test are probably liable to moderate local infection."

The reliability of a negative test as a true indicator of the immunity possessed is convincingly attested by the observation of Park that in spite of the fact that 24 per cent. of all children showing a negative Schick reaction were found to be carriers of virulent diphtheria bacilli, none developed diphtheria, and, furthermore, he has never seen a case of clinical diphtheria develop in a person reacting negatively to the Schick test.

The saving of time and inconvenience and of the expense for antitoxin effected by omitting the prophylactic injection of antitoxin in immune persons is a matter of no small moment among the general population as well as in institutional practice.

II. ACTIVE IMMUNIZATION AGAINST DIPHTHERIA.

In many communicable diseases the greatest and most lasting immunity is that conferred by an attack of the disease, while a transient passive immunity is that produced by antitoxic and other immune serums. When exposure to infection is recent, immediate, or likely to occur within a few days, the prophylactic injection of diphtheria antitoxin is by far the most efficient means for warding off an attack of the disease. It should be borne in mind, however, that the protection afforded by an immunizing dose of antitoxin can be depended upon for a period of only two to four weeks. In the past decade there has been developed a method of producing active immunity in human beings, which is far more lasting, although it requires a considerably longer time to develop, than that produced by antitoxin. The injection of diphtheria toxin partially neutralized with its antitoxin—and, therefore, harmless—stimulates the production of sufficient native antitoxin in the body to cause persons previously reacting positively to the Schick test to react negatively, and to render them immune to an attack of diphtheria.

The development of active immunization by means of toxin-antitoxin mixtures constitutes one of the most notable contributions of medical science to the welfare of mankind. The possibilities of its univeral adoption and application must be apparent when it is realized that by such a means it would be possible to immunize all susceptible persons to diphtheria, thereby preventing the clinical disease. The complete harmlessness of the procedure, and the efficacy of the protection it affords for a period of at least four and a half years have been firmly established by the results of Park's experience in 15,000 immunizations.

1. *The Toxin-Antitoxin Mixture.* The rationale of immunization with diphtheria toxin-antitoxin consists in the production of an active immunity by the injection of small amounts of diphtheria toxin so neutralized with its antitoxin as to be devoid of any harmful or undesirable action. Potent diphtheria toxin is aged until its strength becomes constant, its potency is then accurately determined, and to 86-100 per cent. of the L+ dose (L+ dose equals the amount of toxin required to kill a 250 gram guinea pig in four days, when mixed with one unit of antitoxin) is added one unit of antitoxin. The mixture is so prepared that the dose used, usually one cubic centimeter, contains three L+ doses of toxin with three to three and one-half units of antitoxin. The mixture is subjected to the most rigid bacteri-

ological tests for sterility, and its harmlessness for human beings is determined by animal tests. Guinea pigs receive one and five human doses, respectively and must survive five weeks before the mixture is finally released for distribution.

2. *Dosage.* The toxin-antitoxin mixture as supplied by the State Department of Public Health is prepared in strict accordance with the requirements of the United States Public Health Service. The course of immunization consists of three injections of 1 c.c., each given at intervals of seven to ten days. The injections of the undiluted mixture are made subcutaneously, preferably over the insertion of the deltoid. For children under six months of age, the dose is 0.5 c.c., and three injections are given at seven-day intervals.

3. *Reactions.* A local inflammatory reaction characterized by moderate swelling and some redness and tenderness, may develop at the site of the injection in adults, but this rapidly subsides and causes no inconvenience. At times, in adults, a slight constitutional reaction consisting of slight fever and some malaise may be caused by the injection. This reaction may be due to hypersensitiveness to protein of the diphtheria bacillus, or it may possibly be caused by pepton in the toxin. This allergic condition exists in many adults, but is rarely found in young children. In the latter, accordingly, reactions seldom occur. Park reports that in his large number of immunizations no serious effects have appeared.

4. *Appearance of Immunity.* The immunity produced in response to this method of immunization develops slowly, it may require a period of eight to twelve weeks for a sufficient amount of antitoxin to develop to inhibit the Schick test. Each individual so immunized should be given a Schick test three months after the last injection. The failure of a person to react to the Schick test shows that sufficient antitoxin is present in the body to render that person immune to diphtheria.

5. *Duration.* The use of toxin-antitoxin mixtures is of such comparatively recent introduction that it is impossible at present to determine the full duration of the protection which it confers. From Park's observations it is definitely established that the immunity persists for four and a half years at least, which is the period over which his studies have continued. It is likely that it exists for life; but, be that as it may, the fact that complete protection continues for over four years, makes it possible by applying this procedure to infants to insure children against infection during what would otherwise be the most susceptible period of their lives.

6. *Influence on Reactivity to Schick Test.* When the full course of three injections is given it will be found that within three months after the last injection over 90 per cent. of all individuals previously giving a positive Schick test will give a negative reaction, and that this number will have acquired an active immunity to diphtheria. The remainder should be immunized by repeating the course of injections.

7. *Influence of Antitoxin Injections on Production of Immunity by Toxin-Antitoxin Injections.* It has been found by Zingher that recent administration of diphtheria antitoxin interferes with and retards the development of immunity following the injection of diphtheria toxin-antitoxin mixtures. Whenever, therefore, the course of injections is given to an individual who has recently received diphtheria antitoxin, retests with the Schick reaction should be performed at the end of ten or twelve weeks after the last injection of toxin-antitoxin.

Under no circumstances should the mere fact that a person has received the usual course of diphtheria toxin-antitoxin be relied upon as proof that complete protection against diphtheria has been produced. All immunizations should be controlled by subsequent Schick tests, and all persons reacting positively to the test should be given a second course of injections of toxin-antitoxin.

III. GENERAL CONSIDERATIONS AND RECOMMENDATIONS.

1. All persons over 18 months of age in the entire community should have their susceptibility to diphtheria determined by means of the Schick test, and the reaction which they show should be noted either in institutional records or in the records of the family physician.

2. In infants below 18 months of age the Schick test is not necessary because a negative reaction may give rise to a false sense of security. Very young infants may exhibit a negative Schick test owing to the immunity passively acquired from the mother, but, inasmuch as this type of immunity is transient, it is safer to as-

sume that no child under 18 months possesses permanent immunity.

3. All infants below 18 months of age accordingly should be actively immunized with three doses of 1.0 c.c. of diphtheria toxin-antitoxin mixture, irrespective of the reaction to the Schick test which the infants might show at the time of immunization. The doses should be 0.5 c.c. for babies under six months of age and 1 c.c. for all others.

4. All persons over 18 months of age who give a positive Schick test should be immunized by receiving three subcutaneous injections of 1 c.c. each of toxin-antitoxin at intervals of seven days.

5. All persons immunized by this method should be retested three months after the last injection, and re-immunized if they should by any chance still give a positive Schick reaction.

The medical profession now possesses in the Schick test a simple and reliable means for ascertaining the susceptibility or immunity of an individual to diphtheria; in diphtheria toxin-antitoxin, a safe and sure method for rendering all susceptibles immune; and in diphtheria antitoxin, an effective means for treating the disease. The State, through the Department of Public Health, offers to the physicians of the Commonwealth the biologic agents required both for the Schick test and for active immunization; every facility for the rapid diagnosis of suspected cases; the service of epidemiologists and district health officers to discover foci and to trace the course of infection; and offers a free and abundant supply of potent diphtheria antitoxin. It would seem, therefore, that with these facilities at our disposal, and with the active coöperation and participation of the medical profession in their use and application, children could be permanently spared from this scourge. The only cases of diphtheria occurring in the Commonwealth would be among those individuals who came from without the boundaries of the State, or those who have failed to receive or avail themselves of the means of protection freely offered to them.

Honor for Dr. Jelliffe.—Dr. Smith Ely Jelliffe of New York has been made an honorary member of the Societé de Médicine Mentale de Belgigue at its recent reunion.

INTERNAL DRAINAGE OF ACUTE EARS, AND ABORTION OF ACUTE MASTOIDITIS BY THE USE OF SIR A. E. WRIGHT'S SOLUTION.*

By George A. Leland, A.M., M.D., F.A.C.S., Boston.

Drainage of the middle ear is furnished by Nature through the Eustachian tube. This tube is not an open pipe, but merely a slit in the side of the naso-pharynx leading up to the bony isthmus, the posterior and superior walls of which are formed by cartilage, and inferior and anterior by soft fibrous (fascia) tissue. In hardened specimens at the top there appears to be a small opening which may be the lumen of a very small part of the structure which, in normal conditions may be more or less open. In very early life, the direction of the Eustachian tube is nearly horizontal, assuming a more and more oblique downward direction as life advances. Now the tube is not simply a pipe to allow the passage of fluids either way, but is lined with mucous membrane whose surface cells are ciliated, the direction of whose constant motion is towards the pharynx.

Moreover, the position of the tube and the downward moving ciliae are not the only factors which assist drainage from the middle ear. The tensor palati, which might be called the dilator of the tube as it is continuous with Rudinger's dilator tubae has its attachment to the anterior lip of the Eustachian cartilage and the fascia of the anterior wall, and by its action pulls the whole anterior wall of the tube forward; and the levator palati is attached inferiorly to a part of the lateral plate and to the membranous part of the floor of the tube. By their contractions, these muscles exert a pumping action on the pharyngeal end of the tube with every movement of the velum, as in talking, swallowing, etc. This is very prettily shown by the late Dr. Holmes' naso-pharyngoscope. Through this little instrument may be seen the forward pull of the anterior wall of the Eustachian tube and also a bulge under the mouth, so as to wedge it open. This swelling is described (Quain) as the belly of the levator of the palate. At all events, this pumping action is very well seen to open the tube by the tensor palati and the bulging belly of the levator to push the anterior wall forward and the posterior harder wall somewhat backward. And it may also be seen that if the inner part of

* Read at the fifty-third annual meeting of the American Otological Society, May 31 and June 1, 1920, Boston, Mass.

the mouth (pharyngeal orifice) is obscured by thickened membrane or if it is covered by translucent adenoidal tissue or if the fossa of Rosenmueller is narrowed or obliterated by adhesions or adenoidal masses, this pumping action is much curtailed or abolished.

It is probably true that 95—99% of acute middle ears have their origin in inflammatory conditions of the naso-pharynx, the consequent swelling blocking the Eustachian mouths. I have laid myself open to criticism by saying that, except from trauma, 100% of the children under 12 years of age, with acute ears, have adenoids. By this I do not mean masses of adenoids sufficient to block respiration, but sufficient to diminish or inhibit drainage and ventilation through the Eustachian tubes; and by this is meant sufficient adenoids to prevent this pumping action and to hinder free exit to whatever the ciliated epithelia may bring down.

Hence, as Nature has supplied this mechanism for this purpose, it has long seemed rational to reëstablish these functions when by inflammatory thickening, infection or simply, by hyperemia they are held in abeyance.

Some years ago, in an A. M. A. meeting, a reader,* or speaker, mentioned that Leland did not hesitate to operate on adenoids in acute conditions. For years, it has seemed to me that this is just the right time to operate, especially for acute conditions involving the middle ear, for then the great desideratum is drainage, *cito, tuto, et jucunde.* It may be readily seen that a quick restoration of the above mentioned functions is the best way to bring about drainage; and it especially recommends itself because there is then no way for infection from without, as in the classic operation of paracentesis, after which an acute case frequently requires attention from one to six weeks, with danger of the middle ear becoming purulent, and of infection of the external canal resulting in furunculosis.

This method is simply to clear the region around the Eustachian tube in front and below, but especially in the fossa of Rosenmueller. This evidently cannot be done with any form of a naso-pharyngeal guillotine, because that instrument does not reach the fossae; but must be done with a naso-pharyngeal curette of almost any form, or with the sharpened sterile and alcohol-hardened finger-nail. In using the curette, the contour of the spinal column should be borne in mind, and then with the shank of the instrument in the same side of the mouth, with an outward twist and downward sweep, the posterior wall of the fossa is readily and smoothly cleared: the finger-nail may then be used to finish up (the tactus eruditus). This procedure is usually followed up by a little belladonna or atropia to diminish circulation in the throat. Usually, when the earache is thus treated early, within the first 24—48 hours, the inflammation in the tympanum immediately subsides. But even after three or four days, if rupture of the membrana tympani has not taken place, drainage begins, bulging subsides, and soon the hyperaemia disappears.

With all these acute attacks, it is probable that there is more or less effusion into the tympanum. Hence, after the redness has disappeared, say after five days, it is good practice to blow the drumhead away from the inner wall to prevent adhesions. This may be necessary but a few times for it is probable that the drumhead soon assumes its normal position, because air finds its way into the drum cavity. After five days or so, it may also assist to make a few applications of an organic silver disinfecting and astringent solution to the sides of the naso-pharynx, especially into the wounded fossae, lest adhesions again diminish their width and depth.

Brief mention of a few cases may point this moral, if they do not adorn the tale:

About seven years ago, on a Tuesday, a child of about three years of age, her face suffused with an acute cold, was being hurried away from the clinic. The mother said she had cried with earache two or three nights. Both drumheads were red and markedly bulging. Over a cuspidor, two rooms away from the mother, vociferous lachrymation and futile resistance being at this age a good analgesic, with the sharpened and cleansed finger-nail, the naso-pharynx and especially the lateral recesses were relieved of masses of soft adenoids, accompanied by much hemorrhage—a good derivative—which soon ceased. Two days later, there was no bulging and there has been no more pain complained of; slept well. Two days later, the redness had almost disappeared and the child appeared to the mother about normal. In this case the duration of the earache before treatment had been longer than desirable.

* The Relation of the Rhinopharynx to the Middle Ear and Mastoid. By E. L. Jones, M.D., Cumberland, Md., Jour. A. M. A., Jan. 9, 1915, Vol. lxiv, pp. 115-117.

On November 26, 1913, about 7 P.M., I learned from a pediatrician, that a child was in need of a specialist, for acute ears. I found a child of seven months, both drumheads bulging, on one of which was a considerable bleb. The child, of course, had taken cold; had not slept much the night before, peevish all day, without appetite; in fact, had refused food. I told the doctor that I did not wish to incise the drumheads, as that probably would mean more or less attendance afterwards; but I preferred to get internal drainage. He said he did not know what that meant, but what I wished to do he would sanction. We therefore enveloped the child in a blanket and sheet and, without anesthesia, with Vogel's small curette, the naso-pharynx, and especially the fossae, were freed from a small amount of adenoidal tissue. It was impossible to get my finger up behind the palate. I therefore used the curette to scrape and roughen the surface as much as possible. Hemorrhage slight. Prescribed a slight amount of belladonna to be given when awake through the night. I asked the doctor to make his visit in the morning and to call me if he found things not satisfactory. He found the child sitting on her mother's knee, crying for a second bottle; had been a little restless the early part of the night, but had slept pretty well; no sign of inflammation in either ear. The bleb had broken, but the drumheads were in good position and color; there was no injection to be seen. He expressed astonishment at the condition of the child. I took the precaution to examine her next day. Found the condition of the ears as if nothing had taken place. On the fifth day, I called to inflate the middle ears and found her out-of-doors in her carriage, a blustering December day. I also visited the child next day and inflated the ears, and that was the end of the trouble—otitis media acuta, 24 hours standing; immediate restoration to the normal.

On January 30, 1916, a gentleman in a neighboring city said his family doctor wished to incise one of the drumheads of this little girl of about three years of age, but he preferred to have it done by a specialist. I found the right ear markedly bulging and reddened. This was the ear that was to be cut, and the other was just beginning; therefore if the right had been cut it would have been necessary in a few hours to perform the same service for the other. After a slight argument, the doctor who expressed ignorance of any such procedure, persuaded the father to allow the adenoid operation. This was done as usual with special reference to the region of the tubes behind and below. It was accomplished with a curette, and finger-nail. The doctor afterwards said there was no sign of inflammation the next day and the ears were inflated on the fifth day. I afterwards learned from the father that the family physician was doing the same thing to some of his patients with success.

On the seventh of April, 1915, a child 2½ years of age had complained of an earache two or three days. About the same conditions as above mentioned were found, and the same treatment was carried out. The subsidence of symptoms and restoration to normal conditions did not take place for about nine days and then inflation was necessary twice within a week. Since that time no trouble with the ear has taken place, and she has been remarkably free from colds.

These cases are not the only ones, of course, but are perhaps typical. Whenever an acute middle ear (and also ordinary catarrhal cases) come into my practice this is the treatment followed, if the parents and patients can only be persuaded to allow it.

Of course in the light of modern carelessness as to ears, which, happily, is gradually disappearing, this operation may seem too formidable to parents; therefore we sometimes meet with opposition. This procedure, moreover, while it has brilliant results in the acute cases, is also beneficial for conditions of the middle ears where a chronic process, catarrhal adhesive, or suppurative seems intractable. It is doubtless true there would be many less running ears and many less cases of catarrhal deafness if the restoration of the free Eustachian tube with an efficient pumping action of its muscles could be brought about.

Now, as to cases of abortion of mastoiditis, here drainage comes into play again, and it is time the profession woke up to the futility of trying to drain abscesses through a pinhole, as my colleague, Dr. Borden, has expressed it. It has been my practice for the last six or eight years to drain acute inflammatory conditions of the middle ear involving the mastoid through multiple openings of the membrana tympani and the peripheral walls of the canal. Dr. George P. Sanborn, a pupil of Sir Almroth Wright and our best sero-therapeutist, intro-

duced me to Wright's so-called "drawing" solution. Sir Almroth describes its action as making use of a decalcifying substance (sodium citrate) which stops coagulation of the blood, together with an hypertonic solution of salt, which induces rapid exosmosis. The solution consists of 1% of citrate of soda and 4% salt (chloride of sodium).* An acute mastoid usually shows tenderness and redness and perhaps some swelling over the bone. In this case there is usually a much thickened and reddened drumhead and marked prolapse of the walls of the bony canal, especially superiorly and posteriorly. A small hole through the drumhead usually does very little good, therefore an incision should be made through the posterior segment of the drumhead curving upward and backward on the bony wall of the canal and cutting deep down to the bone. Three other deep incisions are made similarly through Shrapnell's membrane beginning at the posterior fold, upward and out on the canal; another at the anterior fold, another directly above the neck of the hammer. Of course the bleeding is profuse. Sometimes coagulation of the blood will stop sufficient drainage. In order to obviate this, the solution of citrate and salt is poured in warm immediately after the incisions, and with a pledget of cotton in forceps or with a cotton applicator is pumped down into depth of the canal and the bleeding encouraged and clots, if any, wiped away, until the solution is well applied to the incisions. A light gauze wick is then introduced, saturated with the solution, and a dry pad (or two) placed over the orifice. The pad is to be changed as often as wet, but not the wick in the canal. Usually the cotton pad is soaked every 15 miuntes in the next 24 to 48 hours, and it is often astonishing how much serum comes away. The next morning the wick in the canal is changed and the warm solution again poured in; and if the incisions have begun to close they are wiped with a cotton applicator to start bleeding again. This latter procedure I have found almost never necessary. Now this flux is not simply drainage, but we get the advantage of a tremendous welling outwards of a large amount of lymph with its more or less bactericidal action, which power increases as more and more fresh serum is drawn from the blood and washed through the infected region. At any rate inflammatory conditions are usually absent in the course of a day or two.

February 18, 1914. With a Chesterfieldian flourish, a physician of Jamaica Plain brought me a patient, saying, "Ah, Doctor, I have brought you a mastoid!" Man, 29 years old, large, florid, and well-fed; five weeks before, had a cold. Four weeks ago much pain in left. Paracentesis at a hospital two weeks ago. Five days before visit x-rays showed mastoid cloudy. Feverish and chilly up to two weeks ago. Treated by external heat, and whiskey. At visit, temperature 100. Pus in canal, drumhead red, thick, opaque, granulations and a pouting perforation upper posterior quadrant. Tenderness over antrum and posterior border of tip, no swelling nor redness over mastoid. Naso-pharynx treated with solution of silver nitrate 4%; and Rhinitis full strength every hour till dry throat. Nose much engorged, with marked deflection of septum to left. 19th —No pain since yesterday; tenderness over antrum but not at tip. Took rhinitis tablet triturates too few. Two days later, 21st—Pain began at noon on 20th and lasted till 6A.M. today; tenderness and slight oedema on mastoid. Membrana tympani thick, red, bulging. Free paracentesis under local anesthesia. No pus, some blood, soaked in citrate of soda and salt solution. Bloody serum discharged all night Cotton pads changed often; much pain 9 P.M. to 1 A.M. At visit bloody wick removed, serous discharge. Soaked again with same solution; corrosive wick and cotton pads. No pain night of 22nd. Much discharge till 10 A.M. Tenderness nearly disappeared. On 25th, seven days after first visit, no pain for three days, no granulations, pouting perforation absent. Feels well. Two months later hearing about normal. This case, which had trouble four weeks with temperature, cleared up in about five days without mastoid operation, which seemed saitsfactory.

February 2, 1916, a suburban physician telephoned in he was sending me a mastoid case, and he wanted nothing to do with it. Rev. F. H. S., 39 years old, had grippy cold three days. General pain, malaise; yet preached three days before. On the 1st inst., 3 A.M., very severe pain in right ear; broke at 10 A.M. Copious bloody discharge since; at visit, 12 M., pain nearly gone. This A.M., considerable tenderness of mastoid. Holds head bent to right. No digastric pain. A.M.—temperature 99.8° Right

* "The citrate of soda, by decalcifying the lymph, prevents coagulation and scabbing; and the salt, acting by osmols, causes fluid to transude from the blood vessels. Under the influence of this application, a clear lymph wells out and the local conditions rapidly improve." Studies in Immunization, p. 355.

ear otitis media acuta with perforation, brown exudate on upper posterior wall; posterior wall and Shrapnell's membane prolapsed; granular surface under exudate. At 1.30, under ether, posterior segment incised, and Shrapnell's in three places, all out onto and through to bony wall of canal. Wright's solution pumped in, corrosive wick wet in this solution and gauze pad to auricle. ℞, Rhinitis one-half strength every hour. That night rather restless, very copious watery discharge. Evening temperature, 100.5; pulse, 96. Considerable tenderness of tip and hurt to open mouth (tenderness of inner surface of tip). Wick and solution pads renewed. February 4—Discharge less, pads changed less often. Tenderness of tip continued. Evening temperature 99.4; 5th, less swelling of membrana tympani and Shrapnells; less tender tip. Evening temperature, 97.4; 6th: better, less discharge, mastoid tip and digastric tender. Posterior inferior quadrant slightly swelled; paracent. under local anesthesia, slight bloody flow, same solution used (citrate sodium and salt). Went to complete recovery and on the 28th, hearing normal. Membrana tympani shows scar in posterior segment and bright point of adhesion at anterior border of umbo.

It was, I think, McKernon who called attention to prolapse of superior and posterior walls in grippy conditions, after the great influenza epidemic of 1889 and 1890. This case, with that bony involvement and tender tip seemed bound for a mastoid, but subsided in five or six days.

August 3, 1916, F. S., boy, 10 years old, brought by mother from beach. Great swimmer. Night of 29th ult. (5 days before), much earache. Probably got sea water (dilute sewage) into nose and blew it, as is seen so commonly at bathing places, salt and fresh. Next two days treated at home with hot instillations and hot boric irrigations. Next day more comfortable. Today, languid, no appetite, less pain last night than at first. Head held stiffly to right. Temperature 100.3. No pain referred to mastoid. Drumhead bulging, red and thick, especially Shrapnell's and posterior segment. Anterior and posterior tip tender.

As an elder brother had had a mastoid operation 5½ years before parents were much afraid of having another. Hence under primary ether, usual four deep incisions were made. Citrate soda and salt solution pumped in many times as blood clotted very quickly. Few adenoids were stripped from sides of naso-pharynx with curette and finger-nail and grain ⅛ Belladonna extract given every hour. Pads changed frequently that night and next day, no pain, ear tender, temperature 99.8 at noon. Moved from hospital to hotel on fifth. Temperature normal on 8th (five days); and on 22nd, nineteen days after, no discharge, and hearing about normal.

This case seems to have taken considerable time—19 days—but my experience with these cases of infection by sea water (or nasal irrigating solutions) has been such that 19 days doesn't seem long. Here the value of the transudation of lymph by Wright's solution, which may be considered a chemical Bier's method of passive congestion, is well demonstrated.

Let us not forget also the advantages of clearing out the sides of the naso-pharynx, so as to restore ventilation and drainage through the Eustachian tubes.

It may be thought that the duration of treatment of these cases does not indicate any advantage over a simple paracentesis. Of course it is a common experience to cut a bulging drumhead and to have the inflammation subside in a few days; but it must be borne in mind that in cases above mentioned, on account of prolapse of the walls and more or less temperature, and tenderness at the tip of the bone, a mastoid operation seemed very likely in the near future, especially in cases where the inflammatory thickening of the membarna tympani and mucosa of the middle ears was so great as to result in a nipple perforation which is of almost no value as to drainage. One of my late colleagues once said he disliked to see nipple perforations because they were *always fatal.* That may have been so thirty or more years ago, but in these modern days when the mastoid operation is resorted to with much less provocation, if drainage cannot be obtained through the middle ear, it can be through the bone. But by use of Wright's solution and free incisions, it can be accomplished in almost every instance if not delayed too long, *i.e.*, until much pus has formed. Here it has not done so well. And there is a further, and probably the most important, advantage in getting at these cases as early as possible, and that is to stop inflammatory deposit which means hardness of hearing sooner or later.

TREATMENT OF HYPERTROPHIED TONSILS AND ADENOIDS BY RADIUM, A PRELIMINARY STATEMENT.

By Francis H. Williams, M.D., Boston.

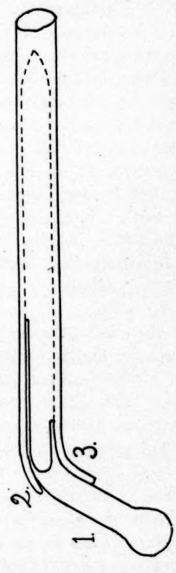
The excellent paper recently published by Drs. Murphy, Wetherbee, Craig and Hussey, entitled, "Induced Atrophy of Hypertrophied Tonsils by Roentgen Ray,"* is interesting and instructive, but treating the tonsils from "under the angle of the jaw" and the adenoids "through the back of the neck" is open to the criticism of exposing to the rays other parts than those it is desired to reach. The rays from radium also act on the lymphoid tissues, of which the tonsils and adenoids are made up to a large extent, and can be applied directly to the tonsils and adenoids, the neighboring parts being protected by lead, that is to say, the radium container is covered with lead except on the side through which it is desired that the rays should issue. When as above, roentgen rays were used, the maximum amount reached other tissues than the tonsils and adenoids; when radium is employed, the maximum radiation reaches the tonsils and adenoids, and the minimum other parts. Another advantage of radium is that the output is constant, and the dosage can be exact.

I have used 50 milligrams of bromide of radium in a flat container, with the rays filtered by 0.83 millimetre o faluminum, held directly against or near the tonsil. The radium should be withdrawn every few minutes, or as often as is comfortable for the patient, until the total exposure of fifteen minutes, more or less as required, has been reached. Improvement follows promptly, but the ultimate results may be expected only after some weeks. Guided by more than seventeen years' experience in the use of radium, it seems to me better not to attempt complete healing by one treatment, for the present at least, but rather to give two or perhaps three treatments at intervals, as patients and conditions differ.

It may prove more convenient to use a container by means of which both tonsils may be treated at the same time. I have devised one to be held midway between the tonsils, which consists, in general, of a disk of lead (not more than 2 cm. in diameter and about 1 cm. thick, more so in the middle) with a hole bored through its centre, somewhat flared at each end, for the exit of the rays, and another bored from the outer edge radially to a little beyond the centre. The tube containing the radium may be slipped into this and the opening afterwards closed by screwing a metal handle part way into it. The uvula, the back of the throat and the parts behind it are thus protected by about 1 cm. of lead. When treating one tonsil only, the opening towards the other may be closed with a plug of lead. Appropriate filters should be used.

* Jour. A. M. A., 1921, Vol. lxxvi, p. 228.

Another instrument, useful to reach parts of the throat that would not be accessible to a larger one, is shown in the cut.



This cut is one-third larger than the actual size. Below 1. is a small bulb at the end of the bent portion of a glass tube, for containing the radium. The straight end is inserted into a metal handle about 30 cm. long, of which only 7.5 cm. are shown, by lifting the spring at 2, and is held in place by a narrow strip of plaster wound around the glass and metal between 2 and 3. The radium is kept in position in the bulb by stuffing the tube with spun glass, and more spun glass is pushed in until the tube is nearly filled, the end being closed with a cork, instead of sealed off as shown in the cut. An aluminum cap, to act as a filter, is slipped over the bulb and then the bulb and bent portion of the tube are enclosed in sheet lead, except the lower end of the bulb. The lead should extend more or less beyond the bulb according to the size of the area to be treated.

Before applying the radium, the throat should be moistened with a suitable solution of cocaine to prevent gagging from the insertion of the container. All instruments should be covered with two thicknesses of rubber, and for this purpose two rubber finger cots are stretched over them and far down on the handle, where they may be secured by a strip of plaster. Of course, fresh cots should be used for each patient.

In using this method I have thus far treated the tonsil only, as the results there may be more easily observed than in adenoids. These may be reached through the nose by a small instrument, carrying radium, from the end of which the rays issue upwards.

Adenoids can also be reached by directing the roentgen rays upon them through the nose instead of through the back of the neck as described in the article referred to above. This treatment might be carried out, for example, by distending the nostrils with a special bivalve speculum, one blade inserted horizontally in each nostril, and by protecting the skin inside the speculum with oxide of zinc plaster and that outside by sheet lead. In this case the length of exposure would be shorter, for children only about one minute, than when the rays are obliged to traverse a large amount of dense tissue, and the risk of burns would be far less.

The disadavantages of operation are obvious. The roentgen rays should be employed only by physicians who have had experience in their use.

It is, of course, too early to make a definite statement concerning the comparative value of operation, roentgen rays, and radium. For adenoids the roentgen rays and radium—treatment by both of which is painless—may each be of service in a special group of patients. For the tonsils, radium, if properly used, I consider the safest and that it will probably prove to be the best treatment for many patients.

While not coming within the title of this paper, it is noteworthy that after treatment by radium, I have observed striking improvement in acute and sub-acute tonsillitis.

THE ENERGY REQUIREMENTS OF GIRLS FROM 12 TO 17 YEARS OF AGE.

By Francis G. Benedict, and Mary F. Hendry, Boston.

[From the Nutrition Laboratory of the Carnegie Institution of Washington, Boston, Massachusetts.]

(Continued from page 222.)

SELECTION OF SUBJECTS.

Recognizing the importance of securing subjects in groups, squads or troops, preferably subjects known to each other or with at least general unified interests, we presented the whole problem to the Massachusetts Council of Girl Scouts through Mrs. James J. Storrow, whose interest made further relations possible. It would be difficult to express adequately our appreciation of the wholly extraordinary degree of coöperation, at great personal sacrifice of time and labor, on the part of several of the Girl Scout leaders, particularly the Director, Miss Alice Sanford, and the leader of Troop 11, Miss Marion C. Moreland. To secure the consent of the parents to their girls participating in tests of this kind and to assemble successfully the several groups of girls was a feat in education, diplomacy, and organization which is rarely observed, and the successful accomplishment of the same is a striking comment upon the extraordinarily high character which the Girl Scouts hold in public opinion, particularly in the opinion of the parents of the large number of girls who volunteered to coöperate in these tests.

It was decided to begin our study with the older girls first, because we felt that, psychologically, the younger girls would be much keener to carry out tests which had been already made with older girls. Secondly, the plan of collecting a group of girls for an evening and a night at the Laboratory could be developed better first with the more mature rather than with the younger girls. This order proved most successful.

All the girls were selected on the basis that they were "presumably in good health and normal." Finer differentiation as to physical condition has not thus far been made in metabolism work; it may have to be done, but it is of less importance with the group system than with the study of individuals, for even in the extreme case that an individual girl might have a basal metabolism 50 per cent. above normal, with a group of 12 girls this would affect the average value of the entire group only by 4 per cent. Still, every effort was made to select girls who were presumably in good health.

In forming our groups we attempted to secure uniformity, first, as regards age, and in the age groups attempted to obtain further uniformity by limiting the range of weight and height, but with the best of intentions it was almost impossible to adhere to this latter point. Even as regards uniformity in age, the basic ground for classification, certain groups included girls with a wider age range than was desirable, and while the average age of the groups differed by approximately one year, the fact must not be lost sight of that in certain instances girls a little too old or a little too young for this age designation were included. It was soon found that, although we could draw for the major part from two of the largest

troops of Girl Scouts in Boston, there were not sufficient girls of uniform age to permit sharp specifications as to height and weight, and so very considerable height and weight variations entered into all the groups. Here, again, however, emphasis must be laid upon the fact that with the group system such variations play a relatively minor rôle, and while there is a distinct disadvantage in grouping all the girls under one average figure, thus losing their individuality, so to speak, there is a distinct advantage in that abnormalities, even if of considerable magnitude, are almost without effect upon the average figure. Finally, at the critical prepubertal and pubertal ages of 13 and 14 years attempts were made to secure groups in which the most decisive criterion of puberty in females, namely, menstruation, had or had not appeared. With all of these attempts at grouping certain variations unavoidably crept in.

PROGRAM.

The squad, in Girl Scout uniforms, usually arrived at the Laboratory in charge of a Scout leader not far from 5 P.M., and sat down to supper, served in the library of the Laboratory, in conjunction with the experimenters and with the squad leaders at 6 o'clock. As many of the girls had formerly been in Girl Scout camps, this part of the evening was looked upon as a "lark," a revival of the summer camp and "mess" table. The girls had been requested to eat nothing after 2 P.M., or if they had inadvertently eaten confectionery or fruit, to report it. There was no instance where such were eaten in sufficient magnitude to affect the results in any way. After supper the table was cleared and the girls were given an evening's entertainment consisting of educational and entertaining motion picture films, interspersed with short talks upon the object of the Girl Scout experiments. There was likewise a brief description given, illustrated with motion picture films, of the methods of study of the heat production of infants and young children. Opportunity was afforded the girls to visit various parts of the Laboratory, where apparatus was demonstrated to them. During the evening, also, a group photograph of the squad with squad leaders was taken.

From 10 to 10.30 P.M., the girls prepared for bed, at which time records of weight and height were obtained. To avoid the error due to clothing each girl was weighed with a previously weighed sheet, so that the nude weight was available. After being weighed and measured, the girls entered the respiration chamber, popularly termed the "bungalow," and in the later experiments at least were again weighed with the nightdress on, just prior to going to bed, on scales sensitive to 10 grams. At this second weighing, the exact time was recorded, and each girl was cautioned to wear the next morning, when being weighed again, exactly the same handkerchief, hair ribbon, hair pins, wrist watch, or any other accessory that she had on at the time. All these weights were taken without slippers, the purpose being to secure the true loss in body weight throughout the night by making another weighing under exactly the same conditions the next morning before the bladder was emptied, and thus secure data with regard to the insensible perspiration.

Immediately after being weighed, the girls went to their separate beds and quieted down for the night. Instructions were then given as to the morning routine, the chief new factor of which was the counting of the pulse rate by two of the experimenters. Specific directions were given the girls as to how to raise the cover of the chamber immediately, in case of urgent need of leaving. It is worthy of special note in this connection that on the nine nights, in which, all told, 95 girls participated, in no instance was it necessary to take a girl out of the respiration chamber and in no instance did a girl hesitate to go in, thus testifying to the perfect organization of the Girl Scouts and the confidence that they had in their leaders. After these instructions the cover of the chamber was then closed, the lights were put out, black curtains drawn over the glass windows, and the subjects cautioned to remain quiet and go to sleep as soon as possible.

To minimize the correction for residual carbon dioxide necessary to be made for the carbon-dioxide measurements of each period, we took advantage of the first hour, when the subjects were more or less active and restless, some of them awake, to allow the carbon dioxide to accumulate, and did not begin the true metabolism measurements until later. At the end of approximately an hour the ventilation was started, a sample of the residual air taken for the calculation of the carbon dioxide in the

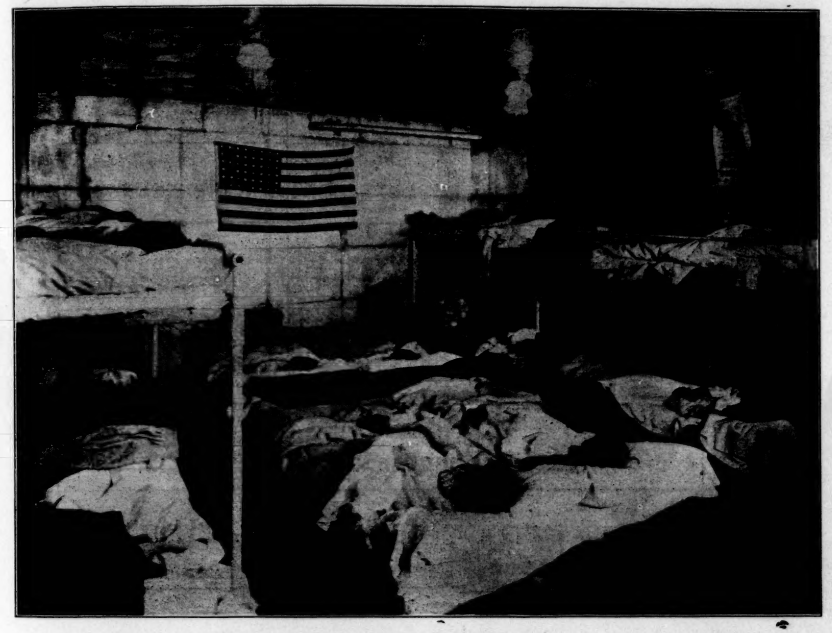


FIG. I.—INTERIOR OF GROUP RESPIRATION CHAMBER, NUTRITION LABORATORY OF THE CARNEGIE INSTITUTION OF WASHINGTON, BOSTON, MASS.
TWELVE GIRL SCOUTS IN BED, PRIOR TO BEGINNING TEST.

chamber, and the first experimental period entered upon.

Periods of one-half hour each were usually made until approximately 2.30 A.M. From there on the periods were lengthened to an hour, and on the nights when the respiratory quotient was determined all ventilation was shut down for another hour and a half, to allow the residual carbon dioxide to accumulate. The total carbon-dioxide production during these periods with no ventilation was always determined by analysis. In the last hour or hour and a half the ventilation was again started and the usual procedure followed. At 6.30 A.M. the cover was usually opened, the chamber rapidly ventilated with a high speed blower, and two experimenters entered the chamber quietly and took the resting pulse rate of each of the subjects. After the pulse rates had been taken, the subjects were called in numerical order, were weighed carefully, the time being recorded, and then left the chamber and dressed, preparatory to breakfast. Breakfast was served in a considerable variety and unlimited quantity to the group as a whole, with absolutely no restrictions, and the girls then left the Laboratory with their squad leader for their respective homes.

A relatively large percentage of the girls volunteered to come at any subsequent date that we could use them, and on the nights when special groups in the 13 and 14-year-old ages were desired, advantage was taken of their offer, so that some of the girls appeared in more than one group. Furthermore, in certain groups where one or two girls were distinctly outside the age range for the specific group, they were requested to come again in the age group under which they would more closely fit. Thus, as a matter of fact, three girls actually appeared three different times in certain groups.

PROBLEMS STUDIED.

Pulse Rate. The opportunity of studying groups of young, normal girls, resting quietly, sound asleep, made us desirous of securing all possible physiological data on them, since information with regard to the physiology of

TABLE III.—INDIVIDUAL AND AVERAGE VALUES FOR AGE, BODY WEIGHT, HEIGHT, AND PULSE RATE[1] OF GIRLS.

Date and subject number[2]	Age		Body weight (without clothing)	Height	Pulse rate	
					First count	Second count
1920	yrs.	mos.	kgs.	cms.		
March 12-13						
67	13	8	36.3	148	70	—
68	13	1	47.4	164	95	92
69	12	9	46.1	157	76	80
70	13	0	34.6	149	53	56
71	12	5	35.8	139	80	75
72	12	10	38.9	152	87	81
73	13	0	39.9	148	85	77
74	12	4	46.0	153	77	76
75	12	9	41.6	152	66	60
76	12	4	43.7	152	77	94
77	12	10	34.5	146	78	81
78	13	4	47.4	158	69	71
Avg.	12	10	41.0	152	76	77
March 19-20						
44	14	1	44.5	162	76	76
45	13	6	55.7	157	71	70
39	14	4	59.9	162	70	74
79	13	8	50.6	161	—	—
80	14	3	56.6	161	74	84
81	14	3	55.7	166	84	83
82	14	3	44.8	154	84	79
83	13	9	52.5	164	103	88
84	13	10	41.0	158	77	90
85	13	9	38.8	151	94	85
86	13	10	71.5	168	75	72
87	14	6	48.6	162	70	67
Avg.	14	0	51.7	161	80	79
April 9-10						
35	13	11	57.2	171	76	78
44	14	1	45.1	162	98	94
39	14	5	62.2	162	73	78
88	14	9	37.0	157	73	77
89	14	6	41.4	154	66	73
90	14	4	45.3	152	72	80
91	13	7	46.7	160	70	66
92	14	7	33.8	145	88	95
93	13	3	40.8	149	92	89
94	13	8	40.8	144	72	82
95	13	9	35.8	151	71	70
Avg.	14	1	44.2	155	77	80

TABLE III.—INDIVIDUAL AND AVERAGE VALUES FOR AGE, BODY WEIGHT, HEIGHT, AND PULSE RATE[1] OF GIRLS. (*Continued.*)

Date and subject number[2]	Age		Body weight (without clothing)	Height	Pulse rate	
					First count	Second count
1920	yrs.	mos.	kgs.	cms.		
Jan. 23-24						
35	13	8	58.7	169	88	82
36	13	7	33.3	145	84	81
37	14	3	50.7	160	65	70
38	13	7	55.3	158	68	62
39	14	2	59.2	161	80	77
40	14	3	52.7	161	85	88
41	13	3	49.2	153	86	88
42	12	10	42.2	165	102	99
43	14	1	41.7	150	78	76
44	13	11	44.2	160	96	87
45	13	10	56.7	169	82	80
46	13	4	55.7	157	82	85
Avg.	13	8	50.0	159	83	81
Feb. 13-14						
35	13	9	58.2	169	80	76
36	13	8	33.7	145	74	74
47	12	10	41.7	149	96	88
38	13	8	56.2	158	70	—
48	13	8	40.2	143	90	82
49	14	0	41.7	157	72	70
50	13	2	42.7	148	96	90
51	12	11	36.7	152	86	84
52	12	8	41.7	154	56	64
53	12	6	40.7	154	80	80
54	13	0	36.2	151	94	96
46	13	5	54.2	157	—	79
Avg.	13	4	43.7	153	81	80
March 5-6						
55	12	6	40.7	155	96	83
56	12	6	37.7	157	88	84
57	11	7	38.7	150	88	75
58	12	6	27.7	144	80	82
59	11	9	36.7	143	74	73
60	12	1	39.7	143	76	74
61	12	5	37.2	146	86	76
62	12	4	40.7	150	84	78
63	12	8	37.7	146	91	88
64	11	7	43.2	154	85	88
65	11	11	49.2	153	86	100
66	12	5	44.7	154	98	90
Avg.	12	2	39.5	150	86	83

TABLE III.—INDIVIDUAL AND AVERAGE VALUES FOR AGE, BODY WEIGHT, HEIGHT, AND PULSE RATE[1] OF GIRLS. (*Continued.*)

Date and subject number[2]	Age		Body weight (without clothing)	Height	Pulse rate	
					First count	Second count
1920	yrs.	mos.	kgs.	cms.		
Jan. 2–3						
1	15	9	61.1	164	87	90
2	16	11	58.0	154	68	78
3	16	3	53.1	153	60	63
4	16	9	73.0	168	64	66
5	18	0	57.0	160	58	65
6	17	3	54.1	171	87	80
7	17	3	64.2	168	75	76
8	17	1	52.9	171	79	75
9	16	3	61.0	162	89	85
10	17	1	51.6	160	71	66
11	17	8	55.6	165	93	89
12	17	4	55.6	161	77	77
Avg.	17	0	58.1	163	76	76
Jan. 9–10						
1	15	9	60.6	164	91	92
13	15	9	40.4	165	82	84
14	15	5	62.8	158	—	74
15	16	0	49.1	162	69	67
16	15	7	49.7	167	75	80
17	15	3	50.6	167	72	74
18	15	7	77.5	172	60	60
19	14	10	57.1	166	79	66
20	16	6	50.1	157	74	66
21	15	8	47.0	157	72	72
22	16	6	53.8	159	62	59
23	16	3	45.1	157	80	65
Avg.	15	10	53.6	163	74	72
Jan. 16–17						
24	16	0	43.5	153	84	82
25	15	5	45.8	157	78	78
26	14	7	50.5	160	60	60
27	14	5	45.1	159	99	96
28	14	4	57.3	150	85	84
29	14	8	54.5	161	88	84
30	14	7	45.5	156	95	86
31	15	3	61.5	170	86	89
32	14	5	47.9	156	84	80
33	15	1	44.0	156	88	88
34	14	6	52.8	167	98	86
Avg.	14	10	49.9	160	86	83

[1] The records of pulse rate were obtained between 6.30 A.M. and 7.00 A.M., while the girls were lying quietly, prior to rising and having breakfast.

[2] Subject numbers underlined represent girls who have *not* reached puberty.

young girls is extremely scarce. Even with so commonly and so readily observed a factor as pulse rate almost no information is available as to the resting pulse of normal girls. The resting pulse rate of these girls after a night of quiet, deep sleep inside the chamber was, therefore, counted each morning.

Insensible Perspiration. The total loss in body weight due to the vaporization of water from the lungs and skin and to the oxidation of organized tissue in the body is the so-called "insensible perspiration." This is measured by noting the true loss in weight over a number of hours. This measurement involves that all clothing and accessory appurtenances must be the same at the beginning and end of the observation and that during this time either no urine and feces are passed and no food and water taken, or else that they are properly corrected for. Obviously this measurement does not call for a respiration chamber and was only an incidental observation.

Gaseous Metabolism. The prime object of this whole series of experiments was to measure not the pulse rate or the insensible perspiration, but the gaseous metabolism, and from that compute the energy transformations of young girls. For this purpose the respiration chamber was devised, and the whole experimental plan was dominated by this main idea. The measurements of the gaseous metabolism began not far from 11 o'clock at night and continued, uninterrupted, until 6.30 in the morning, in periods ranging in duration from one-half to one hour, or, at times, one and one-half hours. From these data we are able to se-

cure information with regard to two important points. In the first place, from a careful examination of the individual periods we can note the actual minimum carbon-dioxide production throughout the night, or the true basal value, and since all the groups were studied under the same conditions with regard to quantity of food and time of eating and with regard to muscular repose (the girls being sound asleep in bed)* comparable basal values for the different ages can be secured. Secondly, the measurement of the total carbon-dioxide production during the night enables us to compute the actual energy consumption during the average night in bed, that is, the total energy requirement for from 8 to 10 hours, the ordinary "in bed" period of young girls. This of itself is of considerable importance as it represents the energy production for 10 of the 24 hours of every child's life. In our discussion of results, therefore, it is natural that emphasis should be laid upon the measurement of the gaseous metabolism, with special reference to the basal or minimum, as well as the total energy production during bed rest. This last is also not without clinical and hospital interest as indicating the metabolism of patients in bed.

DISCUSSION OF RESULTS.

Normality of Girls Studied. Since this study was purposely designed to represent normal girls as nearly as possible and to fill the need for normal material, particularly in connection with basal metabolism, it is important to examine our data anthropometrically, to establish the approximate degree of normality of our girls when compared with so-called standards for age, weight and height established by other investigators. In Table III are given the individual and average ages, weights and heights of our girls, together with subject numbers and dates of observations.

While it is not wholly inconsistent to consider the average weight of girls 12 years of age or younger, it is quite clear that with the higher ages the weight increment per year is by no means so great as it is with the lower ages, and consequently one would expect that 12-year-old girls as a whole would run more nearly to an average weight than 17-year-old girls. Nevertheless, since our study deals solely with groups and the individual, as such, is completely lost in the measurements, we have deemed it advisable to consider only the average weights and heights for the various groups and we will compare these with the average weights and heights of girls in other well-established series of measurements. Accordingly in Table IV we give the average weights and heights of our girls, arranged according to decreasing ages, and for comparison with them have also given the weights and heights for the corresponding ages as obtained from the smoothed curves representing the girls measured by Wood and the private school girls of Benedict and Talbot.

(To be continued.)

* As early as 1895, Sondén and Tigerstedt (Skand. Arch. f. Physiol., 1895, Vol. vi, p. 149), in their monumental research on the metabolism of children, emphasized the fact that to determine the influence of age and body size upon the intensity of the metabolism, the best results will be obtained by studying the metabolism during deep sleep.

Book Review.

Pulmonary Tuberculosis. By EDWARD O. OTIS, M.D. Boston: W. M. Leonard, 1921.

We are glad to see this new and enlarged edition of Dr. Otis's book. While technically it is called a new edition, it is practically a new book, so much material having been added to it that was not in the first edition.

The great fault that the reviewer finds with many treatises on tuberculosis intended, as announced in the preface, for the general practitioner or student, is that they contain too much, with the result that the person looking for information is lost in the multiplicity of detail. Dr. Otis's book does not have this fault. Sufficient detail is given to answer every purpose, and yet the main object in view is never lost sight of.

The value of the book is increased by having added to it the "Diagnostic Standards" prepared for the Framingham Demonstration, the diagnostic theses of Dr. Lawrason Brown, and likewise a number of illustrative cases. His chapter on the examination of soldiers for tuberculosis, along with the "Simplified Rules for Tuberculosis Examination," by Major Stoll, are likewise a welcome addition.

The paper is good, the print excellent, and the division of the subject matter into plainly labeled paragraphs, makes it easy to read and facilitates the finding of any one special point. As a writer of medical English, Dr. Otis has always ranked high. The reviewer gladly recommends this book as one which will prove of distinct value to students and to teachers, and to the medical profession at large.

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PSYCHOLOGY AND MEDICINE.

IN its relation to medicine, the science of psychology presents a number of aspects which might be developed further to the distinct advantage of the medical profession. Although the significance of psychological phenomena in medical problems has been recognized in a general way, the more specialized study of psychology in its medical relations, as a study of experience and behavior from a biological point of view, presents a subject comparatively new. In this connection, Dr. Robert M. Yerkes, in an interesting discussion of "The Relations of Psychology to Medicine," before the American Association for the Advancement of Science, has formulated suggestions in regard to the introduction into medical schools of a science which shall deal with the more direct problems of psychology and medicine, a science for which the name "psychobiology" has been proposed.

Hitherto, physiology has neglected those functional aspects of human life which may be designated as behavior, experience, and mind. These phenomena, if methods could be devised for their exact study, would constitute appropriate material for physiological observation; through our increased knowledge gained by the science of psychology, we are now in a position to gain such facts, which are of considerable theoretical and practical importance.

Of the various aspects of modern psychology, there are three which have a particular significance from the standpoint of medicine: introspective psychology, genetic psychology, and behaviorism. The observations of introspective psychologists in regard to experience and its expressions, cannot be disregarded by medicine; genetic psychology and its study, by both objective and subjective methods, of behavior and experience, when the method of comparison is applied to materials of observation, is associated even more intimately with medical science. But of still greater significance to medicine is the recent development of so-called "behaviorism," which extends application of the objective methods of physiology to all types and aspects of human activity and experience by subjecting to scientific analysis and measurement instinctive, habitual, and voluntary actions. By the further development of psychobiology, there could be studied by introspective psychology, genetic psychology, and behaviorism, phenomena which should be valuable to medicine.

If it be granted that the science of psychobiology be of sufficient importance to medicine to justify its introduction in medical schools, it remains to be considered how this might be undertaken. Dr. Yerkes has suggested the following outline of activities as practicable in the larger medical schools, provided a thoroughly competent biologically trained psychologist is available:

I. There could be presented initially, as a voluntary course, if it is not expedient to add a new subject to the curriculum, a lecture, demonstration and laboratory course in psychobiology, which should acquaint medical students with the principal facts and laws of human behavior and experience and with the more important methods of observing and measuring these phenomena.

II. A groundwork in psychobiology having been prepared by the general course, opportunity should be afforded interested students for more intensive training in the use of psychobiological methods. This should provide alike for training in the methods of practical meas-

urement and for psychobiological research. In connection with the latter, investigation might be undertaken of problems formulated in the lecture course in connection with such topics as the analysis of instinctive activities; the development, modification, and integration of habits; the nature and significance of ideational types; the discovery of peculiarities or defects of behavior and experience. Similarly in connection with practical psychobiological measurement, the medical student might be given opportunity to utilize or develop methods of measuring aspects of behavior and experience in relation to diagnosis and treatment. Important types of practical psychological tests might also be exhibited in their relations to medical aspects of hygienic, industrial, and educational problems.

III. As an extension of psychobiology toward psychiatry, special lectures and laboratory exercises dealing with atypical, abnormal, or pathological behavior and experience, could be provided. These might ultimately be expected to develop into a systemic course in psychopathology, which should be carefully correlated with the established medical instruction in neurology and psychiatry. In this same connection, as a method of supplementing such practical and research activities as are referred to in the preceding paragraph, psychobiological methods might be placed at the service of the neurological and psychiatric clinics, for psychology has already developed a considerable array of methods whose diagnostic value in neuropsychiatric practise has been definitely established.

IV. Another important field of service for psychobiology is preventive medicine and hygiene. Here research in connection with the characteristics and variations of behavior and experience which are significant of undesirable or dangerous nervous or mental tendencies, is particularly in point, although didactic lectures might also be offered to advantage. Thus psychobiology might be utilized increasingly as the partial scientific basis of mental hygiene.

Dr. Yerkes is convinced that there exists a need for developing psychobiology as a basic medical science; it is a project to which the profession may wish to give thought and consideration.

MEDICAL NOTES.

NORBURY SANATORIUM APPOINTMENT. — Dr. Samuel N. Clark, Associate Division of Neurology and Psychiatry, University of Illinois, Medical Department; also Clinical Psychiatrist to the Illinois State Psychopathic Institute, and Secretary of the Chicago Neurological Society, has been appointed Psychiatrist to the Norbury Sanatorium, Jacksonville, Illinois.

RECEPTION IN HONOR OF DR. WILLIAM W. KEEN.—In honor of the eighty-fourth birthday of Dr. William W. Keen, a dinner and reception given by the medical profession of Philadelphia, was attended by six hundred physicians and friends on January 20. Among the speakers were Dr. George de Schweinitz, Dr. William H. Welch of Baltimore, and Dr. J. Chalmers DaCosta of Philadelphia. A volume containing addresses and letters was presented as a tribute to Dr. Keen by Major-General Merritte W. Ireland, Surgeon-General of the United States Army, and a life size bust of Dr. Keen in army uniform, by Samuel Murray, was presented by Dr. William J. Taylor of the College of Physicians.

TRIBUTE TO DR. ROENTGEN.—The twenty-fifth anniversary of the discovery of the roentgen ray by Dr. Roentgen has been celebrated in Germany. Dr. Roentgen retired last year from the chair of experimental physics at the University of Munich.

MISSOURI SOCIETY FOR MENTAL HYGIENE.—At the organization of the Missouri Society for Mental Hygiene at St. Louis on January 13, the following officers were elected: President, Dr. M. A. Bliss; Secretary, Dr. J. F. McFadden; Treasurer, Dr. J. E. W. Wallen.

HOSPITALS FOR DISABLED SOLDIERS. — There has been passed recently a bill authorizing the construction of five hospitals, at an estimated cost of $12,500,000, for the benefit of men disabled in the war. An additional $500,000 is to be made available for converting buildings into hospitals at Walla Walla, Washington, and Fort McKenzie, Wyoming. The bill also authorizes the Secretary of the Treasury to leave subject to appropriation by Congress, the proposed $3,000,000 hospital to be built by the State of New York. Although the specific location of the five hospitals has not yet been determined, one is to be in the Central Atlantic Coast States, one in the Great Lakes region, one in the Central Southwest, one in the Rocky Mountain States, and one in Southern California. Three hospitals, it is planned, would be used for the care of men suffering from mental and nervous disorders, and two for the treatment of tubercular patients.

THE CHALMERS COLLECTION.—A valuable collection of medical books, chiefly on tropical diseases, and including some incunabula of inestimable value, has been presented by Mrs. Chalmers to the Royal Society of Medicine, and is to be known as the "Chalmers Collection," in memory of her late husband, Dr. A. J. Chalmers. The sum of £500 has been given by Mrs. Chalmers for the furnishing of a room in which the books are to be kept. About sixty volumes from Dr. Chalmers' library have been given to the Royal College of Physicians of London.

PLANS TO PREVENT TYPHUS.—At a recent conference of federal officials, new methods were considered for safeguarding the people of the United States from the introduction of typhus from Europe. New regulations are to be adopted as a result of a survey of the situation in New York as revealed in a report from the Assistant Surgeon-General. The prohibition of admission of immigrants from typhus-infected districts of Europe is considered unwarranted in view of the precautions already taken and contemplated.

BOSTON AND MASSACHUSETTS.

THE REPORTING OF LETHARGIC ENCEPHALITIS.—Announcement has been made that after March 1, physicians throughout the State will be required to report to the State Department of Health all cases of lethargic encephalitis which come to their attention. This action has been taken in order that the Department may have a better opportunity for investigating the disease. During the month of January, forty-three cases of this disease have been reported to the Health Department, and eleven have been reported during the first half of February. Investigation thus far has failed to show whether or not the disease is communicable; it is important that all possible information be obtained in regard to it in order that measures may be adopted for its prevention. On February 12, five cases of the disease were reported in Holyoke, and four cases have been reported from Springfield since January 1.

MASSACHUSETTS HOMEOPATHIC HOSPITAL.—Owing to the rapid growth of the various sections of the Out-Patient Genito-Urinary Department of the Massachusetts Homeopathic Hospital, there are several vacancies on the staff. Included in the Genito-Urinary Department are various sub-sections: diseases of kidneys and bladder, diabetes, gonorrhea in male and female, syphilis. Anyone interested should apply for further information to Dr. Henry M. Pollock, Supterintendent, Massachusetts Homepathic Hospital, or to Dr. S. H. Blodgett, Chief of Clinic, 520 Beacon Street, Boston.

WORK OF THE BOSTON DISPENSARY.—The tabulated reports of the Boston Dispensary show that during the year 1920, 152,508 visits were made by patients to the Dispensary, of which 111,126 were in the morning clinics and 41,382 in the evening pay clinics for working people of moderate means. The Dispensary district physicians made 6,171 home visits on patients too ill to go to the Dispensary.

On February 1, 1921, Dr. Herman A. Osgood was appointed Consultant Roentgenologist and Chief of the X-ray Department. The X-ray Department is open daily from 9 A.M. to 5 P.M. and on Monday and Friday evenings from 6 to 8.30.

On March 2, a special evening clinic was started in the Gynecological Department, of which Dr. Malcolm Storer is the Chief, for the special study of dysmenorrhea and sterility. This clinic is under direct charge of Dr. Samuel R. Meaker. For the present it will be conducted Wednesday evenings from 6 to 8.30, and will be on the same pay basis as the already established evening clinics at the Dispensary.

HARVARD GRADUATE SCHOOL OF MEDICINE WORCESTER EXTENSION COURSE.—In arranging for the Extension Course this year, it seemed worth while to vary the plan somewhat by offering a longer series of lectures by a single authority. The popularity of Dr. Frederick T. Lord's previous lectures led him to be invited to give the course this year, the dates and subjects of which follow:

March 16. Suggestions regarding history taking and physical examination. Special tests in certain groups of cases.

March 23. Certain aspects of pulmonary disease, diagnostic hints and therapeutic suggestions.

March 30. Lobar pneumonia and serum treatment.

April 6. Diagnosis and treatment of cardiac disease. Cardiac irregularities.

April 13. Diagnosis and treatment of nephritis. Tests of renal function.

April 20 Immunity. Vaccine therapy. Lumbar puncture. Examination of spinal fluid.

Those who desire to enroll for the course, should forward check for ten dollars to Dr. William F. Lynch, 390 Main Street, Worcester. If the enrollment is sufficient, continuation of the course will be arranged as heretofore. Place of meeting will be announced before the first lecture.

WEEK'S DEATH RATE IN BOSTON.—During the week ending February 26, 1921, the number of deaths reported was 213 against 364 last year, with a rate of 14.66 against 23.48 last year. There were 35 deaths under one year of age against 48 last year.

The number of cases of principal reportable diseases were: Diphtheria, 63; whooping cough, 12; scarlet fever, 60; typhoid fever, 8; measles, 109; tuberculosis, 48.

Included in the above, were the following cases of non-residents: Diphtheria, 12; scarlet fever, 6; measles, 28; tuberculosis, 13.

Total deaths from these diseases were: Diphtheria, 8; scarlet fever, 1; measles, 6; tuberculosis, 12.

Included in the above, were the following non-residents: Diphtheria, 3; tuberculosis, 2.

Encephalitis lethargica: cases, 4; deaths, 2.

MORBIDITY AND MORTALITY IN BOSTON.—Officials in the Health Department of the City of Boston are very much concerned with the report of eight cases of typhoid fever in one week. Since the first of the year, and up to the end of the week, closing February 19, only seven cases, in all, were reported; but in the week of February 26 there were eight more cases.

Diphtheria deaths numbered eight. This was the highest number of the winter. There were 67 cases of sickness from that dread disease reported. Measles also reached its highest in deaths, claiming six. There was an epidemic of measles, for 109 cases were reported.

Cancer deaths dropped from 24 for the preceding week to 14. There were four deaths from erysipelas, one from scarlet fever, 13 from lobar pneumonia, and seven from bronchopneumonia, 15 from Bright's disease and nephritis, and 28 from heart disease. Almost one-third—73 in all—were more than 60 years old. Eleven deaths were accidental or caused by violence.

Two deaths from encephalitis lethargica were reported. Of the 213 deaths, 135 were those of persons born in the United States, 51 were children under five years old, and 103 died in public institutions.

Correspondence.

REPORTABILITY OF ENCEPHALITIS LETHARGICA.

Boston, February 18, 1921.

Mr. Editor:—

At a meeting of Dr. Eugene R. Kelley, Commissioner of Public Health, and the Public Health Council of Massachusetts, it was voted to declare encephalitis lethargica a disease dangerous to the public health and, as such, reportable.

This action was instituted in order that further investigation might be made of the incidence, etiology and mode of transmission of this disease. A special pamphlet on encephalitis lethargica will be distributed to the physicians of the state.

This condition, up to this time, has been voluntarily reported by the physicians of the state, and about 75 cases have been investigated by the Department. Of this group there were but five children, the remaining cases being adults.

Of 28 cases cared for in certain of the Boston hospitals, an increase in the cell count of spinal fluid has been noted, varying from 15 to 50 mononuclear. In this small group there has not been a single incidence of secondary infection or multiple cases in a household, or any localized grouping of cases.

The Department is also circularizing the physicians of the state regarding typhus fever, calling to their attention the need of greater vigilance in the differentiation of the exanthematous conditions. While no great apprehension is entertained that typhus fever is to be introduced into Massachusetts, the unusual increase of immigration of course makes this possible.

By direction of the Commissioner of Public Health,

Very truly yours,

B. W. CAREY,

Director of Division of Communicable Diseases.

NOTICES.

A clinical meeting in the auditorium of the Beth Israel Hospital, Wednesday evening, March 9, at 8.15.

"Cardio-Vascular Diagnosis," Dr. Paul White.

Discussion: Dr. S. A. Levine, Dr. Harry Linenthal. Dr. Joseph H. Pratt.

Dr. Hyman Morrison will preside.

E. GRENVILLE CRABTREE, M.D., *Secretary.*

THE HARVEY SOCIETY.—Saturday evening, March 12, at 8.30 o'clock, the eighth lecture of the series will be given by Dr. S. B. Wolbach, Associate Professor of Pathology and Bacteriology, Harvard University, on "Typhus Fever and Rickettsia," at the New York Academy of Medicine, 17 West 43rd Street, New York City.

HARVARD MEDICAL SOCIETY.—Next meeting in the Peter Bent Brigham Hospital Amphitheatre (Van Dyke Street entrance,) Tuesday evening, March 15, at 8.15 o'clock.

Program by members of the staff of the Massachusetts General Hospital.

1. Oxygen Inhalation in Conditions of Oxygen Want. A. T. Barrach.
2. Blood Pigment Metabolism. Chester Jones.
3. Electrocardiographic Evidence of Progressive Myocardial Degeneration. C. S. Burwell.
4. Local Chemical Factors with a Bearing on Resolution and Recovery in Lobar Pneumonia. F. T. Lord.

Medical students and physicians are cordially invited to attend. CYRUS C. STURGIS, *Secretary.*